

14th Annual Aagaard Lecture

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I am truly grateful for the honor of being asked to give this 14th George and Lorna Aagaard Lecture and really for several reasons. First and foremost is to know that there is a place where a Dean is held in high esteem. Second is the opportunity to visit this medical center which has attracted so many of my old classmates and colleagues; Ben Belknap, John Neff, Bob Wilkens, Marv Turck and so many others. To those of us who live on the other side of America, it has been a place to which friends and faculty left but from which few ever seemed to return. Finally, it is a privilege to pay homage to the architects and creators which the Aagaards are and have been.

To create, to pioneer and to dare what has not been done before as they have done is a stimulating and ultimately fulfilling experience. I think that what is often less reflected upon are the vicissitudes and the uncertainties, the defeats, the near disasters and the self-doubt as events take an unexpected turn. With most of the waking moments of one so engaged devoted not to what is going right but usually to what is going wrong, it is often difficult to maintain that necessary degree of optimism and equilibrium that serves to sustain a dream. To do that over many years, indeed over

decades, is beyond the capacity of all but a very few. I pay homage to those who can do it, and particularly to the Aagaards.

I should like to begin if I may with a quotation which basically sets the theme of what I would like to discuss with you. If we may have the first slide. This is from Mohatma Gandhi:

I am hard-hearted enough to let the sick die if you can tell me how to prevent others from becoming sick.

In saying this, as he did shortly before his death in 1948, Gandhi made a statement which is fully applicable even today to many of the peoples in the developing world.

Our own industrialized world stands in contrast. Most of the major infectious diseases have disappeared, although AIDS is now proving a challenging exception. People are living considerably longer and with fewer disabilities. Deaths among mothers and infants are rare. What principally has accounted for these changes? I think we need to reflect on this. As we reflect on this we realize it is principally better nutrition and housing and sanitation, pure water and sewage systems, pasteurization of milk, child spacing and immunization. Not until perhaps very recently has it really been reflected upon as to the role we as clinical physicians have played, and I am afraid that, when it is all toted up, actually clinical medicine has not played a major role in the major changes in morbidity and mortality in the industrialized countries.

As Gandhi recognized, most of the critical measures required far

more funds and organizational structures than were presently available to any developing country. Of those few which were feasible one must recall that suitable family planning measures were really not available until the 1960's and, until recently, immunization against any other disease except smallpox was unknown. Very few countries performed anything but smallpox vaccination. Until the global eradication program began most of the vaccines in use were of borderline quality or altogether ineffective and the instruments used were very painful. However, after the war, the developing countries imitated the industrialized world and indeed were encouraged to do so by many bilateral assistance agencies. Most of the funds were indeed expended for hospitals, for major health centers, for drugs and equipment. With transport what it was and with the limited personnel available, few were served. The needed costs for treatment for the tidal wave of illness which they faced exceeded all of their budgets. Under the best of circumstances the measures, had the drugs been available, could really have had only a marginal effect on morbidity and mortality. Nevertheless the provision of curative care has dominated the agendas of so many of the developing countries with little being done to prevent disease.

Let me give you a very pertinent example of this. In 1972 I was in West Diza Bijon in Iran. At that time Iran was experiencing a major epidemic of smallpox -- estimated to be between 10 and 20 thousand cases -- hidden by the government, but they were desperately afraid. In fact, Shiraz near Persepolis where the great

celebrations were going on was heavily afflicted. I finally was permitted to go to Iran, and we went to West Diza Bijon, the center of the problem. This happened to be the World Health Organization demonstration center for primary health care. Very lovely health centers were set up. So we made stops at a number of the health centers, and I asked the head of the health center in place after place what they were doing about smallpox vaccinations. Were they vaccinating everybody who came into the center? Were they vaccinating only those who didn't have a vaccination scar? The reply very simply was, "Doctor, we have so many sick people we don't have time to vaccinate." Indeed, in WHO's demonstration center for primary care, no vaccination was being performed at all! The government of Iran mobilized special teams to undertake vaccinations. This, I think, demonstrates something of the emphasis and something of the concern that the developing countries have for curative medicine of their budgets. Under the best of circumstances the resources are very limited.

This situation has begun to change. The smallpox eradication program in many ways can be seen to have played a vital role in the process. Prevention and community-based programs are beginning to assume a proper role to complement the curative care side. I think few have appreciated how much has happened in just the last ten years. Enormous changes have occurred in the developing world, and some of them I will describe. Indeed much, much more is possible. Moreover, the lessons we are learning I think have some implications for all of us in the United States.

What has occurred is perhaps better understood by giving you something very briefly on smallpox and its history. This I will recapitulate very briefly before describing what has happened since and what else we can expect. Let me just say a word about smallpox. The disease is caused by a virus; this may be the only electron micrograph appearing on a postage stamp, but indeed it is that. That is a picture of the smallpox virus. It was transmitted from person to person. After direct contact 10 to 12 days elapsed. The individual then came down with a high fever which would persist for two to four days. The individual often would take to bed and then a rash developed, a very severe rash. This is a picture of an ordinary case, not a particularly severe one. As the pustules subsided, the individual developed pitting scars like this man and indeed that is a picture of the man after recovery. Those two pictures are the same individual. About 20% of individuals who contracted smallpox died. There was absolutely nothing that could be done in therapy. Following recovery, blindness occurred in many.

Smallpox is presumed to have arisen in Asia, (maybe in Africa but probably in Asia), perhaps 10,000 years ago. It spread across India and China and later it spread in the 1800s into Europe as that continent became populated enough to accommodate continuing spread of the disease. Indeed the death rates were so high that until some smallpox control began to be achieved in the late 1700s, the process of urbanization did not take place. So urbanization, population growth, the industrial revolution and smallpox control all occurred more or less together. In Central Europe, the disease

was sufficiently severe that it was common practice not to name a child until that child had recovered from smallpox. In the sixteenth century, smallpox came to the Americas. For reasons unclear, the Indians of the Americas seemed unusually susceptible to the disease. There are well documented outbreaks of major proportions along the eastern seaboard of the United States, with 70 to 80% of the entire population dying of the disease. The Spaniards carried smallpox to Mexico and Peru. Numerous deaths occurred. The deaths among adults were so great that the agricultural part of the culture collapsed. This led to difficulties in maintaining the cities, and indeed this was the end of the great Aztec and Incan civilizations.

The vaccine for smallpox was discovered by Edward Jenner, an English country physician, in 1796. It was our first vaccine. It is very interesting as to how the pertinent observations came about. It was that the milk maids were greatly admired for their complexions. The folk tales of the times suggested it was because they had contracted cow pox. You recall from literature that the complexion of milk maids was greatly praised, and it was indeed because they were not scarred by smallpox.

The lesion was a lesion like this on the hand. Jenner took this material, inoculated a boy by the name of James Phipps and from that when the pustule developed, he inoculated others and showed that the vaccine protected against the disease. It was difficult to sustain the virus by transferring it from arm to arm, and it was

difficult to spread it widely. So for many, many years smallpox was partially controlled in the areas where there was enough organization present, a health organization or other organizations, to continue to propagate the vaccine this way. Mainly the industrialized countries of the world were able to control the disease. In the developing countries there was little done at all. Smallpox was sufficiently widespread so that in 1924 there was a convention on diseases which should be subject to quarantine regulations. This is from a Swiss delegate at the time, (1924), who said that smallpox had in reality no place in an international convention. It was not a pestilential disease in the proper sense of the term: It was in effect a disease that existed everywhere. There was probably not a single country in which it could be said that there were no cases of smallpox. This for a disease for which a vaccine had been present for 125 years--and still this was the situation resting as to how one pertinent observations came about.

It was the...
What was being done indeed. There were many hospitals being built, some for smallpox alone, and there were many smallpox wards. An interesting one was this one, on the Thames; this was in London at the turn of the century. It was a smallpox hospital floating on a barge. England maintained smallpox hospitals until 1975. They had six of them which they kept ready to be opened in case smallpox patients were brought into the United Kingdom. Germany built two new ones in the 1960's. There was great fear of the disease. Tremendous fear. Indeed in the United States we were not doing a very good job ourselves in controlling smallpox. We recorded nearly

30,000 cases in the mid-1930's.

Finally in 1959, a decision was made by the World Health Assembly to eradicate smallpox. This was a proposal made by Vice Minister Victor Stanoff of the Soviet Union who appeared at the World Health Assembly held in Minneapolis that year and with great glee quoted Jefferson to justify smallpox eradication being undertaken. It was a nice coup by Soviet scientists. Indeed it was accepted. Some assistance was provided, but progress was very disappointing. Basically we followed a defensive strategy at that time. The United States' last case occurred in 1949. Until 1971, however, we maintained routine vaccination. Children had to be vaccinated at the time of entry to school. Fifteen million people were being vaccinated every year in this country in 1971, for a disease that had not occurred in this country for 22 years! We insisted that each person traveling present a vaccination certificate attesting to vaccination within the preceding three years. All travelers had to present that in this country and around the world. The costs of this were approximately \$150 million per year to the United States. This was an estimate developed by the Centers for Disease Control-- a lot of money being spent for hospitals and defensive strategy but very little being done to get at the heart of the problem.

So as we came to 1967 the situation was that those countries in red were those where smallpox was endemic. That year it was decided by the World Health Assembly to undertake an intensified program for which \$2.5 million was voted. There was a great debate as to

whether it was going to be \$1 million or \$2.5 million. Some delegates thought that WHO could not spend \$2.5 million, maybe \$1 million would be enough. If you think about it, with 50 countries involved, \$2.5 million actually amounted to only \$50,000 being allotted to each country, not a large sum of money by any stretch of the imagination. Approximately 1 billion people lived in those countries, and 10 to 15 million cases were occurring that year.

The strategy that was undertaken was twofold. One was to undertake vaccination widely in those countries, and the second was to try to detect cases and to contain them. This picture was from the Manual as it first came out; every case is in some way a failure of the program--failure to protect through vaccination and/or failure to prevent spread. Continuing epidemiological analysis of cases permits the program to be monitored and permits corrective measures to be applied. Indeed from this the concept that every case was a failure really set the tone for the program because we sought then to try to get identified-- reported-- every case that occurred.

As we were to discover, only about 1% of all cases were being reported. What finally was done in most areas to simplify this was to put two or three people in a vehicle and have them visit every hospital and every health center and to get them to report once a week whether they had cases or didn't have cases. Gradually, bit by bit, they began to report. As they reported cases, it was then possible to go out, isolate a patient, vaccinate in his immediate vicinity and so stop transmission. Because smallpox spread on a

continuing person to person basis it had to keep going if it was going to be sustained. If indeed you found a case, you could isolate the case and keep it from spreading and you stopped, you broke, its chain of transmission. So the effort was essentially that of breaking chains of transmission.

As the program began, one of our major problems was with the vaccine. We had assumed that there would be a lot of vaccine in use and that probably it would be of good quality. We needed 250 million doses a year and, if we spent our entire budget, it would not quite buy enough vaccine for the program. We decided that there was a simple solution. It was to buy no vaccine at all--to seek this through contributions and to help developing countries produce their own vaccines. Canada and the Netherlands volunteered to test the vaccines, and we set out to test all vaccines used in the program. It was the first occasion when an international agency applied itself to testing everyone's vaccines and approving them or not approving them. This was not without a few problems, I can say. When we tested them, we found that less than 10% met accepted international standards. Some of the vaccine from the Soviet Union proved to be inadequate. I flew to the Soviet Union, we talked it over and indeed they agreed they had problems. They closed down some laboratories and, following that, they set up a central testing facility to independently test the vaccine. So did France which had never had a central testing facility until that time. So did Indonesia. So did India. Indeed some of the vaccine from the United States did not meet accepted standards. That I can say was

probably the most difficult time--trying to explain to the laboratory concerned and the Food and Drug Administration that U.S. vaccine did not meet international standards! We were trying to be even handed. There was no doubt about that.

So the program moved ahead, and it moved ahead quite well. By 1970 this was the picture, not too different except in this area here. This was an 18 country program undertaken by the Centers for Disease Control with support by the Agency for International Development. Some of the countries with the highest incidence of smallpox moved very rapidly and very successfully although they were poor. It was a tremendous stimulus to us in the other parts of the world. In 1973 the Americas were free, almost all of Africa was free, leaving only Ethiopia and this block of countries in this area vaccines and we got due to this... program. It was the first occasion when an international agency Why such rapid progress? Many people assumed there was a whole army of vaccinators out there moving like a swarm of ants from village to village. Not so. Our entire staff in Kenya numbered 40. The staff in Rowanda, 12. The staff in all of Afghanistan, 120. In Ethiopia, we had 85. Not very many people. Those were the total national staffs. What did we find? We were very surprised to find that all of the countries had large numbers of health workers. Some reasonably well trained but poorly supervised if at all. Some doing curative medicine if they had drugs but other than that doing very little. Yet, when one was able to provide them some training, some direction and some vaccine, the response was incredible. We got a

lot of support from the health staff that was there. We found that we could achieve a very great deal with small cost. Indeed the cost in many of the countries for eradicating smallpox ranged from two to about ten cents per head!

By 1973 we said that there were only two remaining areas, and one says "only". But this amounted to 700 million people! It was the area where smallpox was most persistent. It was moving constantly with the people moving by bus and train. The strategy in Africa did not work in India. Without going into the details of this, what was set in motion by the team that was there and with the government of India was a search strategy whereby 120,000 people were mobilized to visit initially every village in India and eventually every house in India within a one week period! If one looks at this and thinks about it and thinks of mobilizing a program to visit every house in the United States in a one week period, it is a fairly formidable task. India was two and one half times larger. Indeed they did it. It took almost a year before the system worked well, but indeed it was done. We used a WHO recognition card where workers went from house to house showing the card saying, "Have you seen a case like this? If so, please report it." Our international staff working at this time were very few. Again, not an army. In Geneva there were six of us on the professional staff. That is all there were at the maximum. In the field at most we had 100 international staff. The countries themselves were really doing the job. The staff was of an incredible quality, and I would like to cite just a couple of examples to illustrate this.

I remember arriving in New Dehli on January 1, 1974. The staff in New Delhi had asked for more money, \$500,000. We really needed to keep the India program going. It was really beginning to gather momentum. But where to get \$500,000? That was a lot of money. It was very difficult for us to get even that amount of money from donors. I arrived in India that day, and we had four staff. One was Bill Foege whom many of you know. Bill had a severe herpes zoster infection, was in great pain and in fact still has a scar below his eye from that episode. Nicole Grassay was a French lady who had renal lithiasis and was in such pain she was sitting with a hot pad on her back. Our Czechoslovakian epidemiologist had a severe fungal infection of his foot, he was literally on crutches and eventually wound up with surgery for it. Lastly was a man by the name of Lawrence Brilliant who had severe atypical pneumonia and had one side splinted; he could hardly breathe. I said, "you're asking for more money to intensify the effort. Here's my senior staff, which doesn't look to be in very great shape." There was a long pause, then I think it was Bill Foege who said, "Well, we have thought a lot about this. We decided it can't get worse so its going to get better. Give us the money, we will do the job."

The second story relates to June of 1974, during probably the darkest days of the program. In northeastern India there was a state of Behar where we had never seen smallpox spread like it had in that area. Twenty-five percent of the villages were infected. We didn't have the staff to even contain the outbreaks. It just seemed

to be going wild. At about this time floods began along the river Ganges, and it flooded extensively. Hoards of refugees poured out spreading smallpox everywhere. In the southern part of the state (the state was 60 million people), famine had occurred and there were groups providing help there for, again, refugees. At about that time the railroads went on strike, so we began shipping vaccine by air to try to keep the program going. Then the airlines went on strike. About this time it seemed like nothing else could go wrong and then the health workers went on strike! I was with Bill Foege at the time in Patna. It was 120 degrees; it was absolutely miserable. Every two weeks they had been trying to publish a bulletin for all the staff throughout India, presenting something positive, something optimistic. At this time I said to Bill, "what in heavens name do we put out at this time?" Bill, for those who know him is perennially an optimistic person. He thought a long time and he said, "We can turn the graph of cases upside down and publish it. It is the only thing I can think of that is positive!" The staff worked through that summer in incredible temperatures and during the monsoon, and they broke the back of smallpox.

In August of 1975, we had our last case in Asia. Only Ethiopia remained in the red. The program went rapidly there and finally, on the 26th of October, 1977, the last case occurred. Ollie Milan was a 26 year old cook from Mercus, Somalia. Interestingly, he was a hospital cook who had been a smallpox vaccinator prior to this time but nobody had thought to vaccinate him! That was the irony of the

last case. Years of work went on after this to be sure there were no more cases and then finally the notes from the plenary session of the World Health Assembly in May of 1980 declaring solemnly that the world and all its peoples had won freedom from smallpox and recommending that smallpox vaccination be discontinued in every country and that no country now require vaccination certificates from international travelers. Indeed this is what has happened.

For the developing countries this was a very meaningful achievement. They had successfully eradicated a disease with little external support--in either international staff or in funds. In fact, the average amount of money spent each year was \$8 million. As I calculate it, that is just about enough to keep the Johns Hopkins Hospital operating for one week. That is the global cost. In the course of this, whole wards of hospitals were no longer needed for smallpox patients. Indeed there were some smallpox hospitals which were transformed for other uses. To many in the developing countries it is apparent that they themselves, with their own resources and their own manpower, could do a very great deal more than they had believed. So in 1974, with much discussion, we proposed to the World Health Assembly what is called an expanded program of immunization. That is, to provide to children throughout the world the DPT (diphtheria, pertussis, tetanus), poliomyelitis, and measles vaccines and BCG, the tuberculosis vaccine.

Why this program? I think as we looked at it and talked with colleagues in the countries, we recognized that trained health

manpower was not the limiting factor in undertaking the programs. There was a recognition that when one got community support, one got people involved, and that when you are able to go out with preventive services throughout a community and get that support, then an enormous amount could be done--not simply dealing with those who happened to come to a primary health center. We recognized, too, that if countries could get further experience in managing a program, supervising a program, distributing a vaccine, that this would be enormous help indeed for other programs. So we thought about this and selected this as probably the next most complicated intervention of a preventive character which might be practical and affordable.

By any standard, immunization is clearly the most cost effective measure. Interestingly, as one thinks about it this is the simplest medical procedure we have. There is no simpler medical procedure we have and none more cost effective. Yet what was happening in the developing countries? In 1974, less than 2% of children were receiving any of these vaccines. In fact one can extend this to almost 1980 and say that even then less than 2% of children were receiving these vaccines. At the same time, one could go into hospitals in Dacca, Manila, Jakarta and find whole wards marked "Tetanus", "Diphtheria", "Whooping Cough", "Measles". So here we were providing enormous curative care facilities for diseases which we could totally prevent. I think again it illustrates we have had an emphasis more on curative care than on preventive care in these countries.

Progress was very slow at first, and then it began to gain momentum. It has become UNICEF's child survival and development revolution, its centerpiece. With this has come a surge of resources. The government of Italy announced that it wanted to bring in \$100 million and could it be spent within 18 months so that it could come back with more! The U.S. contribution has been \$80 million. Canada has come in with \$25 million.

What has happened? The figures here show in the 1970's between two and five percent immunization and here we are in 1985--tetanus at just under 20-30% and up here to 50% with BCG. Actually the figures, if China is included, will show that about 50% of the world's children are now being vaccinated against all these diseases. Rotary International has pledged \$120 million for polio vaccine for this program. Rajiv Gandhi has announced in the past year that the immunization of the children of India will be a permanent memorial to his mother. In El Salvador there have been three truces on three separate Sundays; no shots were fired, and everybody went to the field to vaccinate children. In the Americas, immunization has proceeded rapidly enough that the incidence of polio began to plummet in the early 1980's, and it dropped so fast that a year and a half ago the Pan American Health Organization decided to undertake the eradication of poliomyelitis from the Western Hemisphere. Indeed it is now our belief that this will be accomplished within three years.

We have a second development that has come along which has been of great interest and that is the development of oral rehydration therapy for the prevention of death from diarrhea. This was a simple observation that took a long time to sort out. If you put salt and sugar in water and fed this to children with severe diarrhea, it kept them hydrated and they did not die from the dehydration that normally goes with diarrhea. If you put in salt alone, you did not succeed. If you put water alone you did not succeed. But if you put the two in together you had a remarkable effect in preventing death from diarrhea. In 1975 this program began with UNICEF ordering 1 million packets of oral rehydration therapy salts and sugar, they lasted 18 months. This year 1 million packets are being used every day. That is how rapidly its use has spread. Note that this too, like immunization, has been a community-wide program. It has consisted of teaching mothers, teaching nurses, teaching school teachers and what have you, how to use this salt and sugar solution so that when children begin to get diarrhea, they give them the fluid and keep them hydrated.

The third discovery which likewise promises revolutionary change is more recent and relates to the provision of Vitamin A. This has been a surprising finding, one made just a little more than two or three years ago by Dr. Al Summer and his colleagues at Johns Hopkins. They were working in Indonesia and had two groups of villages--one of which they were giving Vitamin A to and the other group to which they were not. The hope was to prevent blindness and hopefully to demonstrate the effects of Vitamin A in this regard.

One of the controls they were using was to see whether death rates were the same in the two groups of villages to make sure that they were comparable populations. As they began to add up the numbers, they found that where they had given Vitamin A the deaths had fallen precipitously. They couldn't quite understand what this was all about. They completed the analysis, and it showed a 35% decrease in death rates among children under the age of 5 receiving Vitamin A--hardly believable. They went back and in the villages which got Vitamin A they found that not all children actually received Vitamin A, only some of them. Once that was corrected for it was perfectly obvious the 35% figure was wrong. The decrease in death rate for the children receiving Vitamin A actually was 60% to 70%! In various ways, these studies have now been repeated in India and in Tanzania. There are now studies going on to see how widespread marginal Vitamin A deficiency is, and it appears to be very wide-spread. How difficult is it to administer Vitamin A? One capsule once every six months, and it costs ten cents! As further studies have gone on, it is apparent that our understanding of Vitamin A and its effects previously focused on the eyes, the blindness and the night blindness that occurs. In fact, Vitamin A appears to have a great deal to do with the integrity of the endothelial lining of the intestine and the lung and that those with Vitamin A deficiency are dying of pneumonia and dying of diarrhea. With Vitamin A, many fewer die of these diseases.

Thus we have three very important changes occurring and an exciting future beckons. Truly a revolution. Right now as one looks at our

biomedical establishment and at what is going on with vaccines, more than 50 vaccines now are under study at various stages--some are being used in the field and some are still in the laboratory. We see possibilities as one begins to look at it that there may be other micro-nutrient deficiencies in addition to Vitamin A. This needs to be explored.

decrease in total cases among...
Finally, one can see great potential for family planning. There is now a broader political and public acceptance of this in most parts of the world than there has ever been. Regrettably those in Washington have not yet understood that and have not accepted it so well. Perhaps enlightenment may come to Washington, D.C. as well some day.

no in Pakistan. There are...
Thus the basic question as we see it over the coming decade: can we identify cost effective methods for disease prevention and health promotion--to provide them throughout a community, not simply to those who happen to show up for treatment of a disease. We need to understand how to do this better. We need to know how to get out there, how to market and merchandise products, terms we were obviously not taught in medical school. We need to draw on skills of others. A lot can be done. We need to think about the provision of health care more broadly than we have, and I think we can.

One asks the question, what applicability does this have to the United States? Well, let me cite a very simple illustration of what

happened last autumn. Miami, Florida; a major epidemic of measles. A survey was done and it established that only 50% of children two years of age had been vaccinated against measles. This in a city with modern American health care and an excess of physicians. Worse than this, 18 cases of measles occurred in children--seventeen of whom had been in a medical institution within the preceding 12 months and had not been vaccinated. But even worse than this, more than 50% of the children had been exposed to measles and contracted it in an outpatient clinic at the hospital or a physician's office. Do we have anything to learn from this or do we have anything to learn about the delivery of preventive services? I think you may wish to draw some conclusions.

I think as we see the field ahead and as we think more about the potential for community-wide interventions, as we see what may be done in our field, we speak of the second public health revolution. I would say if you were looking for an as yet undiscovered growth stock, one might look to schools of public health as an undetected find--if we could just figure out how to arrange a public stock offering! We need to think globally. Health knows no boundaries. This has been forcefully brought home to us by Chernobyl, by the Bopaul incident (?) and _____ Institute in West Virginia, and AIDS. I think to be noted in particular is the fact that for smallpox eradication two indispensable pillars to the program proved to be the United States of America and the Soviet Union, working closely together within the context of a global program of the World Health Organization.

We cannot be complacent. The challenge is to all of us but the time is now. I would like to close with a quotation by Mistral:

We are guilty of many errors and many faults but our worst crime is abandoning the children, neglecting the fountain of life. Many of the things we need can wait. The child cannot. Right now is the time his bones are being formed, his blood is being made and his senses are being developed. To him we cannot answer tomorrow. His name is today.

And today, indeed, we can do very much.

Thank you.

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